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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/898,586	07/03/2001	Valerie L. Gerlach	15966-638CIP (Cura-138CIP)	2872

7590

09/17/2002

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EXAMINER

LI, RUIXIANG

ART UNIT

PAPER NUMBER

1646

DATE MAILED: 09/17/2002

12

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/898,586	GERLACH ET AL.	
	Examiner	Art Unit	
	Ruixiang Li	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 05 August 2002.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 19 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 19 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) 9 are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
 If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 a) ☐ All b) ☐ Some * c) ☐ None of:
 1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
 * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
 a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- | | |
|--------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) <u>7 and 8</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Election/Restrictions

1. Applicants' election without traverse of Group V (Claims 19 and 60) and the amino acid sequence set forth in SEQ ID NO: 24 in Paper No. 11 filed on 08/05/2002 is acknowledged.
2. Applicants' amendment in Paper No. 11 filed on 08/05/2002 has been entered in full. Claims 1-18 and 20-79 have been canceled. Claim 19 has been amended and under consideration.

Priority

3. Acknowledgment is made of a claim for domestic priority under 35 U.S.C. 119(e) to nine provisional applications.

Objections to Disclosure

4. The disclosure is objected to because of an error in numbering the pages: the page for claims should be numbered as page 152, following the end of specification which is numbered as 151. The subsequent pages (after page 152) should also be renumbered. Appropriate correction is required.

Claim Rejections—35 USC § 112, 1st paragraph

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

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The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claim 19 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for determining the presence or amount of a nucleic acid molecule of SEQ ID NO: 23 or encoding the amino acid sequence set forth in SEQ ID NO:24, does not reasonably provide enablement for a method for determining the presence or amount of any other nucleic acid molecules within the genus recited in the claim. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with the claim.

The factors that are considered when determining whether a disclosure satisfies enablement requirement include: (i) the quantity of experimentation necessary; (ii) the amount of direction or guidance presented; (iii) the existence of working examples; (iv) the nature of the invention; (v) the state of the prior art; (vi) the relative skill of those in the art; (vii) the predictability or unpredictability of the art; and (viii) the breadth of the claims. *Ex Parte Forman*, 230 USPQ 546 (Bd Pat. App. & Int. 1986); *In re Wands*, 858 F. 2d 731, 8 USPQ 2d 1400 (Fed. Cir. 1988).

Claim 19 as written recites a method for determining the presence or amount of a genus of nucleic acid molecules. Such a genus comprises a nucleic acid molecule comprising (i) a nucleic acid sequence encoding a polypeptide comprising an amino acid sequence of a mature form of SEQ ID NO: 24/its variant or the amino acid sequence of SEQ ID NO:24/its variant; (ii) a nucleic acid molecule comprising a

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nucleic acid fragment encoding at least a portion of a polypeptide comprising SEQ ID NO:24 or any variant of said polypeptide; and (iii) the complement of any of said nucleic acid molecules.

However, other than the nucleic acid sequence of SEQ ID NO: 23 or encoding the amino acid sequence set forth in SEQ ID NO: 24, the instant disclosure is silent about the specific information on a mature form of the amino acid sequence of SEQ ID NO: 24 and its variants, or the variant of the amino acid sequence set forth in SEQ ID NO:24. The disclosure fails to provide sufficient guidance and information regarding the structural and functional requirements commensurate in scope with what is encompassed by the instant claim. The disclosure fails to show (i) which portions of SEQ ID NO: 23 are critical to the activity of the protein encoded by the claimed nucleic acids; and (ii) what modifications (e.g., substitutions, deletions or additions) one can make to SEQ ID NO: 23 will result in protein mutants with the same functions as the claimed protein. The state of the art (See, e.g., Ngo, et al, *The Protein Folding Problem and Tertiary Structure Prediction*, 1994, Merz, et al. (ed.), Birkhauser, Boston, MA, pp. 433 and 492-495) is such that the relationship between sequence of a protein and its activity is not well understood and is not predictable. Excising out portions of a protein or modifications to a protein, e.g., by substitutions or deletions, would often result in deleterious effects to the overall activity and effectiveness of the protein.

In addition, the disclosure fails to provide sufficient information on how to produce naturally occurring allelic variants from the nucleic acid molecules.

Furthermore, the specification fails to disclose the chromosomal location of these alleles. There is no sufficient guidance or working example on how to make and use the alleles. The prior art does not provide compensatory structural or correlative teachings to enable one skilled in the art to make the alleles.

Accordingly, the disclosure fails to enable a method for determining the presence or amount of such a myriad of the claimed nucleic acid molecules that not only vary substantially in length but also in nucleotide composition and fails to provide any guidance to one skilled in the art on how to use the genus of nucleic acid molecules in the claimed method. Thus, it would require undue experimentation for one skilled in the art to use the claimed method of detecting a genus of the nucleic acid molecules embraced by the instant claim.

7. Claim 19 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention.

The specification discloses a nucleotide sequence set forth in SEQ ID NO: 23, which encodes a polypeptide of SEQ ID NO: 24. However, Claim 19 as written recites a method for determining the presence or amount of a genus of nucleic acid molecules. Such a genus comprises a nucleic acid molecule comprising (i) a nucleic acid sequence encoding a polypeptide comprising an amino acid sequence of a mature form of SEQ ID NO:24/its variant or the amino acid sequence of SEQ ID NO:24/its variant; (ii) a nucleic acid molecule comprising a nucleic acid fragment

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encoding at least a portion of a polypeptide comprising SEQ ID NO:24 or any variant of said polypeptide; and (iii) the complement of any of said nucleic acid molecules. Thus, the claim encompasses a huge number of nucleic acids that vary substantially both in length and nucleotide composition.

The instant disclosure of a nucleic acid of SEQ ID NO: 23 that encodes a single polypeptide of SEQ ID NO: 24 does not adequately support the scope of the claimed genus, which encompasses a substantial variety of subgenera including full-length genes. A description of a genus of cDNA may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus, or of a recitation of structural features common to the genus, which features constitute a substantial portion of the genus. *Regents of the University of California v. Eli Lilly & Co.*, 119 F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997).

First, the claim recites a mature form of the amino acid sequence of SEQ ID NO:24 or its variant. However, the instant disclosure only provides general knowledge on a mature form of a protein. It is silent about the specific information of the mature form of the protein with the amino acid sequence set forth in SEQ ID NO: 24. Needless to say the information provided on the variant of a mature form of SEQ ID NO:24.

Secondly, the claim recites a genus of nucleic acid molecules encoding a variant of the polypeptide set forth in SEQ ID NO: 24. However, the specification merely discloses a nucleic acid of SEQ ID NO: 23, which encode the polypeptide of

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SEQ ID NO:24. There is no allelic sequence information disclosed. There is no description of the mutational sites that exist in nature, and there is no description of how the structure of the polypeptide set forth in SEQ ID NO: 24 relates to the structure of different alleles. Furthermore, the general knowledge in the art concerning alleles does not provide any indication of how the structure of one allele is representative of other unknown alleles having concordant or discordant functions. The nature of alleles is such that they are variant structures where the structure and function of one does not provide guidance to the structure and function others.

Furthermore, despite the claim recites the structural limitation that variation of a variant of a mature form of SEQ ID NO:24 from a mature form of SEQ ID NO: 24 or variation of a variant of SEQ ID NO:24 from SEQ ID NO:24 is less than 15%, the instant disclosure fails to provide sufficient description information, such as definitive structural or functional features of the claimed genus of polynucleotides. There is no description of the conserved regions that are critical to the structure and function of the genus claimed. There is no description of the sites at which variability may be tolerated and there is no information regarding the relation of structure to function. Furthermore, the prior art does not provide compensatory structural or correlative teachings to enable one skilled in the art to identify the encompassed polynucleotides as being identical to those instantly claimed.

Finally, part v of the claim encompasses virtually any random nucleic acid sequence of any length due to the nature of open language "comprising" used in the claim.

Due to the breadth of the claim genus and lack of the definitive structural or functional features of the claimed genus, one skilled in the art would not recognize from the disclosure that the applicant was in possession of the claimed genus.

Claim Rejections—35 USC § 102

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in-

(1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effect under this subsection of a national application published under section 122(b) only if the international application designating the United States was published under Article 21(2)(a) of such treaty in the English language; or

(2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that a patent shall not be deemed filed in the United States for the purposes of this subsection based on the filing of an international application filed under the treaty defined in section 351(a).

9. Claim 19 is rejected under 35 U.S.C. 102(e) as being anticipated by Li et al. (U. S. Patent No. 5,998,164, December 7, 1999).

Li et al. teach a nucleotide sequence encoding at least a portion of polypeptide comprising the amino acid sequence of SEQ ID NO:24 (See attached sequence alignment). Li et al. also teach detection of the presence of mRNA coding for a G-protein coupled receptor comprising obtaining total mRNA from the cell, contacting the mRNA with a nucleic acid probe, and detecting the presence of mRNA hybridized to the probe (bottom of column 15–top of column 16). Li et al. further teach the detection of DNA sequence using a variety of methods (3rd paragraph–bottom of

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column16). Thus, the reference of Li et al. meets the limitation of Claim 19 (part v and vi).

Claim Objection—Minor informalities

10. Claim 19 is objected to because it recites an improper Markush Group. A nucleic acid fragment (v) and the complement of nucleic acid molecules (vi) are structurally different from an amino acid sequence (i-iv), thus they should not be put together in the Markush Group. Appropriate correction is required.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ruixiang Li whose telephone number is (703) 306-0282. The examiner can normally be reached on Monday-Friday, 8:30 am-5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler, can be reached on (703) 308-6564. The fax phone number for this Group is (703) 305-3014 or (703) 308-4242.

Communications via Internet e-mail regarding this application, other than those under 35 U.S.C. 132 or which otherwise require a signature, may be used by the applicant and should be addressed to [yvonne.eyler@uspto.gov].

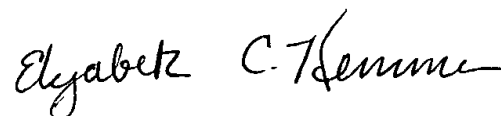
All Internet e-mail communications will be made of record in the application file. PTO employees do not engage in Internet communications where there exists a possibility that sensitive information could be identified or exchanged unless the record includes a properly signed express waiver of the confidentiality requirements of 35 U.S.C. 122. This is more clearly set forth in the Interim Internet Usage Policy published

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in the Official Gazette of the Patent and Trademark on February 25, 1997 at 1195 OG
89.

Any inquiry of a general nature or relating to the status of this application or
proceeding should be directed to the Group receptionist whose telephone number is
(703) 308-0196.

Ruixiang Li
Examiner
September 13, 2002

A handwritten signature in black ink, reading "Elizabeth C. Kemmerer". The signature is written in a cursive, flowing style.

ELIZABETH KEMMERER
PRIMARY EXAMINER